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Martin J. Jacobs

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Ross J. Oehler  
CEPHALON, Inc.  
41 MOORES ROAD  
PO BOX 4011  
FRAZER, PA 19355

EXAMINER

FUBARA, BLESSING M

ART UNIT

PAPER NUMBER

1618

MAIL DATE

DELIVERY MODE

07/08/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                       |                                      |  |
|------------------------------|---------------------------------------|--------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>09/975,350  | <b>Applicant(s)</b><br>JACOBS ET AL. |  |
|                              | <b>Examiner</b><br>BLESSING M. FUBARA | <b>Art Unit</b><br>1618              |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 May 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3,4,8-13,15-43,45-50,55-60 and 63-66 is/are pending in the application.
- 4a) Of the above claim(s) 36-43,56-58,60,64 and 65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3,4,8-13,15-35,45-50,55,59,63 and 66 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.
2. The examiner has reconsidered the rejections and agrees with the applicant that the office action has not explicitly communicated why the ordinary skilled artisan would be motivated to prepare the non-aqueous composition of Nguyen as a liquid. The prior art rejections are the same except for explicit statement as to merits of liquid formulation that is included in the rejections.
3. The examiner acknowledges request for reconsideration and remarks filed 5/18/09. No claim is currently amended. Claims 1, 3, 4, 8-13, 15-43, 45-50, 55-60 and 63-66 are pending. Claims 36-43, 56, 57, 58, 60, 64 and 65 are withdrawn from consideration.

### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
5. Claims 1, 3, 8-13, 17, 18, 31-35, 45-50, 55, 63 and 66 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for organic solvents such as glycerin, propylene glycol, diethylene glycol ethyl ether, propylene carbonate, a medium chain length monoglyceride and polyethyleneglycol, does not reasonably provide enablement for all organic solvents. The specification does not enable any person skilled in the art to which it pertains, or

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with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is scope of enablement.

6. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient number of the above factors are considered below for a *prima facie* case.

1) Nature of the invention:

The nature of the invention in claim 1 is non-aqueous liquid solution comprising modafinil, at least one organic solvent and at least one surfactant. Thus, the modafinil is in solution.

2) Breadth of claims:

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The claims are broad requiring that the modafinil be soluble or dissolve in all organic solvents.

3) State of the prior art and the predictability or lack thereof in the art:

Modafinil is an insoluble drug that is not soluble in all organic solvents. For example, Modafinil is practically insoluble in cyclohexane, sparingly or slightly soluble in methanol or acetone (see column 1, lines 32-35 of US 6,348,500 B1).

Thus, since modafinil is not soluble in all organic solvents, the scope of organic solvents that are enabled for dissolving modafinil is limited to those disclosed in the specification as filed and not to all organic solvents such as cyclohexane, methanol and acetone. It can therefore not be predicted that modafinil would be soluble in all organic solvents as recited in the claims.

4) Quantity of experimentation needed to make or use the invention based on the content of the disclosure:

Since modafinil is an insoluble drug soluble in certain organic solvents such as the organic solvents disclosed and claimed in claim 15, the recitation that modafinil is in solution in all organic solvents requires that the ordinary skilled artisan carryout undue experimentation to determine which of the organic solvents would dissolve the modafinil and which would not.

Therefore, having considered the scope of organic solvents enabled for dissolving modafinil, the quantity of experimentation required to determine which organic solvent dissolves modafinil and the direction provided by the as filed specification, the experimentation required is undue and the organic solvents disclosed in the specification does not meet the full scope of all organic solvents.

The above rejection may be overcome by reciting, even is in a Markush language, the specific organic solvents disclosed and in which the modafinil can go into solution.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 3, 4, 8-13, 15, 17-35, 45-47, 55, 59, 63 and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nguyen et al. (US 5,843,347) in view of Esteve et al. (US 6,566,404 B2 as English translation for WO 99/25329) and Grebow et al. (US 5,618,845) and further in view of Santus et al. (US 5,510,119).

10. Nguyen teaches a pharmaceutical composition comprising particles or microparticles of active ingredient, physiologically acceptable hydrophilic excipient and water (abstract). The

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hydrophilic excipient comprises a polymer component and a water-soluble or water dispersible component that acts as a diluent (column 6, lines 1-5). The polymer component is selected from the group consisting of gum Arabic, xanthan gum, gum tragacanth, alginates, pectinates, polyvinylpyrrolidone, polyethylene glycols, cellulose, carboxymethyl cellulose, cellulose ethers, carboxymethyl chitin, dextran, chitosan, gelatin, acrylic and methacrylic polymers and copolymers, colloidal silica and mixtures thereof (column 6, lines 11-23). The polyethylene glycol meets claim 15. The water-soluble or water dispersible component is selected from the group consisting of lactose, glycoll, mannitol, glucose, sucrose, maltodextrin, cyclodextrins and derivatives thereof (column 6, lines 44-49). The hydrophilic excipients can also comprise surfactants that are capable of oral administration and the surfactants can be polysorbates, sorbitan esters, fatty glyceride polyethers, lecithins, sodium lauryl sulfate, sodium dioctylsulfosuccinate and mixtures thereof (column 7, lines 2-7) meeting surfactant requirements of claims 8-13, 19 and 21-31. The process of preparing the modafinil particles involves homogenization of the active ingredient in solution, suspension, or emulsion and freeze-drying or lyophilization (column 8, lines 15-24) and the modafinil meets claims 1, 3, 17, 18-20, 32-35, 45, 55, 63 and 66. The active ingredient is selected from the group consisting of paracetamol, probucol, piroxicam, phloroglucinol, tiadenol, flerobuterol, modafinil, dexfenfluramine, carbinoxamine maleate, loperamide, lorazepam and mixtures thereof (claim 13). Claims 45-47 recite the properties of the composition; and oral administration is route of administration and route of administration of a composition does not patentably distinguish the claimed composition over the prior art since the composition of Nguyen, a modafinil composition is capable of being orally administered; specifically the lyophilized product of Nguyen contains surfactants capable

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of oral administration (column 7, lines 3-7). Thus, Nguyen specifically envisions oral administration and since the excipients listed are pharmaceutically acceptable, it flows that the modafinil composition of Nguyen is pharmaceutically acceptable and claim 4 is met.

The preparation is lyophilized such that the amount of water is driven to a minimum and would be less than 10% meeting the non-aqueous nature of claim 1 (as gleaned from applicant's specification at paragraph [0020] of the published specification describing non-aqueous composition). Regarding the amounts of surfactant in claims 8, 9, 23-25 and 27-30, and regarding the amount of modafinil in claims 17 and 18, it is within the purview of the artisan to use amounts of surfactants and modafinil in the composition to provide the desired composition. However, Nguyen is silent on the optical character of the modafinil. But it is known in the art that modafinil in the absence of designation of d- or l- is the racemic form comprising of the l- or d- forms. In the absence of factual evidence, the use of the specific l-form of the modafinil is not inventive over the use of the racemic form.

Thus modafinil composition comprising modafinil, surfactant and organic solvent is known according to the teachings of Nguyen as described above. Furthermore, Nguyen teaches using organic solvent such as polyethylene glycol as described above. Nguyen also contemplates oral administration of the composition/formulation to humans (column 7, line 4; column 9, line 60; column 10, line 54). The composition of Nguyen is not a liquid composition. However, it is known to formulate modafinil as liquid solutions according to Esteve (see column 2, line 58; column 3, lines 9-16) and according to Grebow who discloses that modafinil is used to treat narcolepsy, Parkinson's disease, urinary incontinence and Alzheimers disease and that modafinil formulated as tablet, capsule, powder, pill, liquid, suspension or emulsion with

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pharmaceutically acceptable carrier (abstract; column 10, lines 18-23, 42-44). It is also known in the art that oral administration by way of liquid formulation is better accepted by children and the elderly as disclosed in column 1, lines 45-51 of Santus. Therefore, since liquid modafinil formulations are known in the art as noted above, and since modafinil is administrable to Parkinson's disease and Alzheimers subjects and since the liquid formulations are better accepted by the elderly, taking the teachings of the references together and all the critical elements being taught, one having ordinary skill in the art at the time the invention was made would have reasonable expectation of success that the lyophilized product of Nguyen can be successfully reconstituted as a liquid formulation for administration with the expectation that the liquid formulation would be better accepted by subject such as the elderly.

***Response to Arguments***

11. Applicant's arguments filed 5/18/09 have been fully considered but they are not persuasive.

12. Nguyen in view of Esteve:

13. Applicant argues the rejection of claims 1, 3, 4, 8-13, 15, 17-35, 45-47, 55, 59, 63 and 66 should be withdrawn because Nguyen in view of Esteve does not teach all the elements of the claims, and that the combination of Nguyen and Esteve teach away from the claimed invention since Nguyen does not teach liquid solutions but teaches away from liquid solutions by teaching pasty formulations that are viscous, and that Esteve does not cure the deficiency of Nguyen since a liquid composition preparations are incompatible with Nguyen's pasty and extrudable mixture and that the combinations of Esteve and Nguyen would be unsatisfactory for the intended purpose.

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14. a) The examiner agrees with the applicant that Nguyen does not teach a liquid solution and that is why claim 1 is rejected under 35 USC 103 and not under 35 USC 102. The examiner, however, disagrees with applicant with regards to non-aqueous formulation because, Nguyen teaches non-aqueous composition noting that a lyophilized product is essentially not a solution as admitted by applicant in the remarks; also, the specification at paragraph [0020] of the published application defines “non-aqueous” as a composition that contains from 0-10% water so that the lyophilized product of Nguyen meets the limitation of non-aqueous. b) The examiner disagrees with the applicant that Nguyen teaches away from the claimed invention because, solid or liquid formulations are different forms of formulation. The disclosed formulation of Nguyen is the same formulation except that the claimed is a liquid and the disclosed is a lyophilized solid/powder. It is also noted that modafinil have been known to be formulated as liquid. Thus, it would have been obvious to formulate the composition of Nguyen as a liquid or solid with the liquid having advantage over the solid when used by the elderly population that in view of the fact that liquids are easily adaptable to the patient dosage and better acceptable by the elderly patient. Further, Nguyen does not teach against or deride the modafinil formulation in liquid form. Therefore, Nguyen does not teach way from the claimed invention. c) Nguyen does not teach away from combination with Esteve because Nguyen neither teaches that the modafinil composition should not be formulated as a liquid solution nor specifically bares with reasons the formulation of the modafinil as liquid formulation. In the present rejections, Esteve is used to show that modafinil can be formulated as a liquid so that elderly acceptable liquid formulation can be prepared of the lyophilized modafinil formulation for administration to the elderly. Thus, the claimed invention would have been obvious since

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modafinil composition has been known to be formulated in liquid form. d) The examiner disagrees with the applicant that Esteve does not in any way cure the deficiencies of Nguyen because the difference between claim 1 and Nguyen is that Nguyen does not prepare the modafinil composition as a liquid and because modafinil is known in the art to be prepared as a liquid, one would be led to prepare the modafinil composition as a liquid or solid with preference for liquid in light of the easier adaptation to patient's dosage and better acceptability by the elderly population. Nguyen teaches non-aqueous composition because lyophilized product is essentially not a solution as admitted by applicant in the remarks; also, the specification at paragraph [0020] of the published application defines "non-aqueous" as a composition that contains from 0-10% water so that the lyophilized product of Nguyen meets the limitation of non-aqueous. Therefore, the cited art supports a prima facie case of obviousness noting that the requirements of 2141.02 [R-5] I is met and specifically, MPEP 2141.02 [R-5] I says: "In determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); *Schenck v. Nortron Corp.*, 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983). In the present case, modafinil compositions are known in the art, Nguyen does not teach against formulating modafinil as a liquid so that there is an understanding/knowledge that modafinil can be formulated as a liquid, that liquid formulations are adaptable to a patient's dosage and acceptable by elderly and children populations at the time of applicant's invention. Therefore, because the insight into liquid formulations of modafinil is

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well known in the art, and liquid formulations are known in the art in general, formulating modafinil as a liquid would have been obvious to those skilled in the art.

15. Furthermore, applicant's remarks about attacking the references individually at footnote 1 is not persuasive because applicant's present remarks continue to attack the separate references of Esteve and Nguyen and it is again noted that, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The current rejections are based upon Nguyen in view of Esteve and Grebow and further in view of Santus.

16. The proposed modification of Nguyen, that is, the formulation of the composition of Nguyen in liquid form, does not render the intended purpose of Nguyen unsatisfactory as required by MPEP 2143.01 [R-6] V because one of the intended uses of Nguyen is in therapeutics and the formulation of modafinil as a liquid does not render the modafinil unsatisfactory in therapeutic use. The examiner further notes that the examiner has not ascribed liquid to the lyophilized product of Nguyen. However, the examiner acknowledges receipt of Exhibit A and the document is placed in the file,

17. Claims 1, 3, 4, 8-13, 15, 17-35, 45-47, 55, 59, 63 and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nguyen et al. (US 5,843,347) in view of Shah et al. ("Self-emulsifying drug delivery systems (SEDDS) with polyglycolized glycerides for improving in vitro dissolution and oral absorption of lipophilic drugs," in international Journal of Pharmaceutics, 106 (1994), pp 15-23) or Charman et al. ("Self-emulsifying Drug Delivery

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Systems: Formulation and Pharmaceutical Evaluation of an Investigational Lipophilic Compound,” in *Pharmaceutical Research*, Vol. 9, No. 1, 1992, pp 87-93).

18. Nguyen has been described above as rendering obvious the designated claims except that, Nguyen failed to specifically teach liquid formulation containing modafinil. Modafinil is a known water-insoluble drug. However, Charman and Shah individually each disclose the formulation of poorly water soluble drugs using self-emulsifying drug delivery systems (see the whole publications, with emphasis on Table 2 and page 18, left column of the Shah reference and page 88 of Charman). Therefore, taking the general teachings of the references, one having ordinary skill in the art at the time the invention was made would have reasonable expectation of success that adapting the teachings of Shah or Charman in formulating the modafinil composition of Nguyen would produce a self emulsifying formulation of modafinil in liquid form that after oral administration would readily disperse in the stomach to form fine emulsion.

19. Claims 48-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nguyen et al. (US 5,843,347) in view of Shah et al. (“Self-emulsifying drug delivery systems (SEDSS) with polyglycolized glycerides for improving in vitro dissolution and oral absorption of lipophilic drugs,” in *international Journal of Pharmaceutics*, 106 (1994), pp 15-23).

Nguyen in view of Shah is described above as rendering obvious the liquid formulation of claims 1 and 47. Nguyen teaches all the critical elements of the claims except that the formulation of Nguyen is not an encapsulated liquid. But Shah teaches soft gelatin capsules containing liquid compositions of lipophilic drugs (see the entire publication with emphasis on page 18 and Table 2). Therefore, one having ordinary skill in the art at the invention was made

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would have reasonable expectation of success that adapting the teachings of Shah in formulating the modafinil composition of Nguyen, liquid compositions of modafinil encapsulated in soft gelatin capsules would produce a self emulsifying formulation of modafinil in liquid form in gelatin capsules that after oral administration would readily disperse in the stomach to form fine emulsion.

***Response to Arguments***

20. Applicant's arguments filed 5/18/09 have been fully considered but they are not persuasive.

21. Applicant's arguments that the rejections of the claims over Nguyen and Shah or Nguyen and Charman should be withdrawn because Shah and Charman are both directed toward lipophilic compounds while modafinil is not soluble in lipids is not persuasive. Charman and Shah, are relied upon for formulating poorly water soluble drugs as liquid formulations using SEDDS. By the same token, poorly water soluble drugs such as modafinil can be formulated as SEDDS in liquid form noting that the lyophilized product of Nguyen is non-aqueous meeting the requirements for non-aqueous of the claims. Therefore, the combination of the Shah or Charman with Nguyen teaches every element of the claims. While applicant says that the compounds of Shah and Charman are lipophilic and modafinil is not, it is however noted that lipophilic drugs as well as modafinil are water insoluble or hydrophobic. In determining obviousness, a combination of references need not result precisely in applicant's composition. Rather, the question is whether the invention would have been obvious in light of the combination. In the present case, the answer is yes --- the composition would have been

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obvious in light of the combination as outlined in the rejections. See in re Thornberg, 103 F.2d 387 (CCPA 1939).

The examiner acknowledges remarks in footnote 2 at page 6 of 9 of applicant remarks indicating that that the rejection of claim 48-50 were addressed in the remarks of 11/25/08 and applicant's indication also that the rejected claims 48-50 are currently traversed. The examiner also notes that applicant's arguments with respect to claims 1, 3, 4, 8-13, 15, 17-35, 45-47, 48-50, 55, 59, 63 and 66 have been fully addressed above.

22. Claims 1, 3, 4, 8-13, 15, 17-35, 45-50, 55, 59, 63 and 66 rejected under 35 U.S.C. 103(a) as being unpatentable over Nguyen et al. (US 5,843,347) in view of Grebow et al. (US 5,618,845) and further in view of Santus et al. (US 5,510,119).

23. Nguyen has been described above. Nguyen teaches all the critical elements of the designated claims. Nguyen does not specifically teach a liquid formulation.

Grebow teaches a pharmaceutical composition comprising modafinil particles or modafinil pharmaceutically acceptable salt particles (abstract, column 2, column 3, lines 1-55 and claims 1 and 2) and non-toxic pharmaceutically acceptable carrier (column 4, lines 4-1%. Grebow's composition contains an appropriate dosage of between 50 mg and 700 mg of modafinil with a preferred amount of 400 mg (column 4, lines 1 1-18 and column 10, lines 15-17). The modafinil pharmaceutical composition is administered as a tablet, capsule, powder, pill, liquid, suspension or emulsion; the modafinil composition can also be administered topically

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via epidermal patch or administered via direct injection (column 10, lines 18-26). Grebow further teaches a method of altering somnolent state, for example, narcolepsy, idiopathic hypersomnia and related sleep disorders by administering to a mammal a pharmaceutical composition comprising an effective amount of modafinil particles; and an effective amount of the pharmaceutical composition is defined as an amount effective for treating the somnolent state (column 3, lines 56-67). In human clinical trials, modafinil is administered to physically and mentally healthy male subjects (column 5, lines 46 to 56). Regarding claim 67, Grebow teaches liquid or suspension or emulsion composition of modafinil.

The composition of Grebow encompasses stable and unstable suspensions because the prior art does not exclude stable suspensions and thus the suspension of Grebow would be inherently stable. It is also noted that Grebow discloses suspensions containing modafinil and in the suspension modafinil is not crystalline and the particles of modafinil are suspended in the solvent. The composition of Grebow can also be administered as a liquid as described above which meets the limitation of claim 1 requiring a liquid composition. Regarding claims 48-50, the modafinil composition of Grebow is encapsulated and would therefore meet claim 48 with the generic teaching of capsule encompasses hard and soft capsules of claims 49 and 50.

Grebow also teaches administering the prior art composition in clinical trials to mentally and physically healthy male subjects. Orally administering modafinil particles to human subjects (column 5, lines 46-56) would necessarily bring modafinil particles in contact with the aqueous environment in the human subject since human body is mostly water. the prior art is silent on the form of the capsule. Since the prior art is silent on the form of the capsule, hard or soft gelatin capsule, the prior art broad teaching of a capsule encompasses both

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soft gelatin capsule or hard capsule. The expected result would be the encapsulation of modafinil particle in soft or hard gelatin capsule meeting claims 48-50. Therefore, regarding soft or hard capsule, one of ordinary skill in the art is capable of encapsulating the composition in hard or soft in hard capsule or soft gelatin capsule.

Nguyen teaches all the critical elements of the claims. Nguyen does not specifically teach a liquid formulation. Grebow teaches liquid formulation of modafinil. Also Santus teaches that liquid formulations are easily adapted to a patient's dosage and better acceptable to children and elder populations (column 1, lines 45-51). Therefore, one having ordinary skill in the art at the time the invention was made would have reasonable expectation of success that the teaching of Grebow can be adapted to successfully prepare the formulation of Nguyen in liquid form as anticipated by Grebow for anticipated easier adaptation to patient's dosage and better acceptability by the elder population as disclosed by Santus. One having ordinary skilled artisan would have reasonable expectation of success to encapsulate the product of Nguyen for oral administration.

#### ***Response to Arguments***

24. Applicant's arguments filed 5/18/2009 have been fully considered but they are not persuasive.

25. The examiner disagrees with applicant that Nguyen teaches away from the claims because Nguyen while disclosing lyophilized composition, meets the limitation of non aqueous composition as defined by the instant specification at paragraph [0020]. Also, solid and liquid formulations are forms of formulations and it is well known in the art to formulate modafinil in

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solid and liquid forms (see Esteve, Grebow and Nguyen). Therefore, the artisan would have reasonable expectation of success that the formulation of Nguyen would be effectively formulated in liquid form with the advantage that liquid forms are easier adapted to patient's dosage and better accepted by children and the elderly population. With regards to suspensions in deionized water, it is noted that Grebow is relied upon for teaching that modafinil can be formulated as a liquid. Further, with regards to suspension in aqueous medium, it is noted that the claims intend to contact the liquid composition with water or aqueous medium. Therefore, it is unclear where applicant is leading the argument to. The goal is to prepare the composition of Nguyen as a liquid with Nguyen having taught the critical elements of surfactant and organic solvent and modafinil, all of which are present in the non-aqueous formulation. Thus, because Nguyen does not teach against formulating modafinil as a liquid dose, the combination of Grebow and Nguyen does not teach away from the cited claims.

26. Claims 1, 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nguyen et al. (US 5,843,347) in view of Grebow et al. (US 5,618,845) and further in view of Santos et al. (US 5,510,119) and Hochlowski et al. (US 5,589,485).

27. Nguyen in view of Grebow and further in view of Santos have been described above to render obvious the liquid composition of claims 1 and 15. However, the composition of Nguyen in view of Grebow does not contain a further solvent or diluent according to claim 16. But, it is known that liquid formulations contain commonly used inert diluents such as benzyl alcohol, oils, propylene glycol and polyethylene glycols in addition to the active agent according to

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Hochlowski (see column 5, lines 35-43). Therefore, taking the teachings of the prior art references, one having ordinary skill in the art at the time the invention was made would reasonably expect that adding inert diluent such as benzyl alcohol or oils or propylene glycol to the composition of Nguyen as modified by the teaching of Grebow may further stabilize the liquid formulation as a preservative.

### ***Response to Arguments***

28. Applicant's arguments filed 5/18/2009 have been fully considered but they are not persuasive.

29. The examiner disagrees with the applicant that Nguyen and Grebow teach away from the claims as has already been discussed in paragraph 25 above. Hochlowski is relied upon to show the further presence of solvents such as benzyl alcohol as recited in claim 16 and not to support the rejection of claim 1. Hochlowski was not relied upon to teach non-aqueous liquid solution. Nguyen teaches non-aqueous formulation. Grebow is relied upon for teaching that modafinil can be prepared as a liquid so that modafinil non-aqueous formulation of Nguyen would be expected to be successfully prepared as a liquid form.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Blessing M. Fubara/  
Examiner, Art Unit 1618